acid sequence (a) identical to the amino acid sequence shown in Figures 4A-4D (SEQ ID NO: 4) or Figures 23A-23D (SEQ ID NO: 47), (b) encoded by a nucleic acid sequence identical to the receptor-encoding nucleic acid sequence contained in plasmid pEXJT3T7-hGABAB2 (ATCC Accession No. 203515) or in plasmid BO-55 (ATCC Accession No. 209104), or (c) which varies from one of the amino acid sequences of (a) or (b) in terms of the identity or location of an amino acid residue without changing the properties of the $GABA_BR2$ polypeptide.

REMARKS

Claims 208, 210, 213, 214, 221-225, 228-231, and 233-240 were pending and under examination in the subject application. By this Amendment, applicants have hereinabove amended claims 208, 213, 224, and 231. Accordingly, upon entry of this Amendment, claims 208, 210, 213, 214, 221-225, 228-231, and 233-240 will be pending and under examination.

Applicants maintain that the amendments to claims 208, 213, 224, and 231 raise no issue of new matter. Support for the amendments to claims 208, 213, 224, and 231 may be found inter alia in the specification, as originally-filed, on page 21, lines 16-18; Figures 4A-4D; page 25, line 36 through page 26, line 1; Figures 23A-23D; page 33, lines 18-22; page 33, lines 33-37; page 29, line 37 through page 30, line 12; page 80, line 17 through page 82 line 5 and page 82, line 27 through page 83, line 6. Applicants respectfully request that the Amendment be entered.

1. Objection of the Specification

On page 4 of the May 24, 2000 Office Action, the Examiner has objected to the specification because the Brief Description of Figures 19, 20, and 21 fail to refer to the parts of the Figures, e.g. Fig. 19A-I. The Examiner concludes that appropriate correction is required.

In response, applicants amended the Brief Description of Figures 19, 20, and 21 to refer to the parts of the Figures. Accordingly, applicants respectfully request that this objection be withdrawn.

2. Objection under 37 C.F.R. 1.821-1.825

The Examiner maintains that the application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). The Examiner alleges that the application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 because Figure 10 makes reference to two specific sequences, yet only one is accounted for in the Brief Description of the Drawings and these references must contain a sequence identifier of the form: SEQ ID NO: X. The Examiner concludes that appropriate correction is required.

In response, applicants have amended the specification to include the sequence identifier SEQ ID NO: 4 in the Brief Description of the Drawings for Figure 10. Applicants note that the sequence

identifier for the second specific sequence, SEQ ID NO: 55, was added to the specification in the Second Preliminary Amendment and Third Supplemental Information Disclosure Statement filed on January 31, 2000. Accordingly, applicants respectfully request that this objection be withdrawn.

3. Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 208, 210, 213, 214, 221-225, 228-231, 234, and 236-240 under 35 U.S.C. §112, first paragraph. The Examiner alleged that the specification, while being enabling for a method of identifying agonists of the $GABA_BR1/R2$ receptor wherein the $GABA_BR1$ receptor is either of the splice variants disclosed by Kaupmann, et al., referred to in the specification on page 4, and wherein the $GABA_BR2$ receptor is either of the polypeptides disclosed in the instant application as SEQ ID NO: 2, 4, or 47, does not reasonably provide enablement for a method of identifying agonists of the $GABA_BR1/R2$ receptor wherein the receptor $GABA_BR1/R2$ comprises polypeptides other than those recited above. The Examiner further alleges that the specification does not enable any person skilled in the art to which it pertains, or with it is most nearly connected, to make the invention commensurate in scope with these claims. The Examiner concludes that due to the large quantity of experimentation necessary to generate the infinite number of amino acid sequence variants encompassed by the claims and possibly screen the same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity,

the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

In an attempt to advance the prosecution of the subject application, but without conceding the correctness of the Examiner's position, applicants have amended claims 208, 213, 224, and 231. Amended claims 208, 213, 224, and 231 are directed to the mammalian $GABA_BR1/R2$ receptor which consists of a $GABA_BR1$ polypeptide and a $GABA_BR2$ polypeptide, wherein the $GABA_BR2$ polypeptide (a) has an amino acid sequence identical to the amino acid sequence shown in Figures 4A-4D (SEQ ID NO: 4) or Figures 23A-23D (SEQ ID NO: 47) or (b) is encoded by a nucleic acid sequence identical to the receptor-encoding nucleic acid sequence contained in plasmid pEXJT3T7-hGABAB2 (ATCC Accession No. 203515) or plasmid BO-55 (ATCC Accession No. 209104), wherein the amino acid sequence of the $GABA_BR2$ polypeptide may vary from one of the foregoing in terms of the identity or location of one or more amino acid residues without changing the properties. Claims 210, 214, 221-223, 225, 228-230, and 233-240 are all directly or indirectly dependent upon claims 208, 213, 224, and 231. Applicants maintain that the specification provides a detailed description for the amended claims directed to the $GABA_BR2$ polypeptide. Applicants further maintain that the $GABA_BR1$ polypeptide is well-known in the art. As the Examiner noted,

examples of the rat $GABA_BR1$ polypeptide splice variants are disclosed by Kaupmann, et al., which is referred to in the specification on page 4. Applicants note that the sequences disclosed in Kaupmann, et al. are just two examples of the $GABA_BR1$ polypeptides and that further examples of $GABA_BR1$ polypeptides are disclosed by White, et al. White, et al. was cited as Exhibit 11 in the April 26, 1999 Information Disclosure Statement filed in connection with the subject application. Applicants therefore maintain that the $GABA_BR1$ polypeptide should not be limited to the Kaupmann, et al. sequences. Applicants maintain that the specification provides a detailed description for the amended claims and, therefore, maintain this ground of rejection is rendered moot. Accordingly, applicants respectfully request that this rejection be withdrawn.

4. Rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 233 and 235 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Examiner notes that the invention appears to employ novel nucleic acid molecules (i.e., ATCC Deposit number 209104 and 203515). The Examiner maintains that since the nucleic acid molecules are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. The Examiner further maintains that if the nucleic acid molecules are not so obtainable or

available, the requirements of 35 U.S.C. §112 may be satisfied by a deposit of the nucleic acid molecules. The Examiner alleges that the specification does not disclose a repeatable process to obtain the nucleic acid molecules and it is not apparent if the nucleic acid molecules are readily available to the public.

The Examiner notes that applicant has deposited the nucleic acid molecules, but there is no indication in the specification as to public availability. The Examiner further notes that if the deposit is made under the Budapest Treaty, then an affidavit or declaration by applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific nucleic acid molecules have been deposited under the Budapest Treaty and that the nucleic acid molecules will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. The Examiner maintains that if the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that: (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request; (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent; (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; (d) a test

of the viability of the biological material at the time of deposit will be made; and (e) the deposit will be replaced if it should ever become nonviable. The Examiner directs the applicant's attention to M.P.E.P §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. §1.809(d), wherein it is set forth that "specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The Examiner concludes that the specification should be amended to include such, however, applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. The Examiner further concludes that if the Deposit Rules are to be complied with, claims 233 and 235, would be subject to the same scope of enablement rejection put forth above regarding amino acid sequence variants of a $GABA_BR1$ polypeptide.

Applicants' undersigned attorney states herewith that in accordance with 37 C.F.R. §1.808(a)(2) all restrictions imposed by the depositor on the availability to the public of the deposited materials will be irrevocably removed upon the granting of a patent from the subject application. Applicants attach hereto as **Exhibit 1** a copy of the ATCC Deposit Receipt for plasmid BO-55 (ATCC Accession No. 209104) indicating that the deposit was made under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure on June 10, 1997. Applicants additionally attach hereto as **Exhibit 2** a copy of the ATCC

Deposit Receipt for plasmid pEXJT3T7-hGABAB2 (ATCC Accession No. 203515) indicating that the deposit was made under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure on December 10, 1998. Applicants maintain that claims 233 and 235 comply with the requirements of 35 U.S.C.§112, first paragraph and respectfully request that the Examiner reconsider and withdraw the rejection.

In summary, in view of the amendments and remarks made hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds for objection and rejection set forth in the May 24, 2000 Office Action and earnestly solicit allowance of the claims now pending in the subject application, namely claims 208, 210, 213, 214, 221-225, 228-231, and 233-240.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

8/18/00
John P. White Date
Reg. No. 28,678